

**REMARKS**

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

Claims 18 – 35, 39 – 43, 45, 47 – 63, 67 – 71, and new claim 73 are pending, with claims 18, 48, and 73 being independent. Claims 36 – 38 and 64 – 66 have been canceled without prejudice to or disclaimer of the subject matter contained therein as directed to withdrawn subject matter. To expedite prosecution, claims 44, 46, and 72 have been canceled herein without prejudice to or disclaimer of the subject matter contained therein. Claims 18 and 22 have been amended to even more clearly recite and distinctly claim the present invention. New claim 73 has been added. Support for the amendments and for the new claim may be found throughout the specification, especially in the original claims as-filed. Therefore, no new matter has been added.

***Claim Rejections under 35 U.S.C. § 112, Second Paragraph***

Claims 18 – 35, 39 – 63, and 67 – 72 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

With regard to claim 18, the Examiner alleges that the claim is indefinite due to the definition of R”, in combination with the proviso that R’ and R” are not both amide. In response, to even more clearly recite and distinctly claim Applicants’ invention and to expedite prosecution, claim 18 has been amended to remove the proviso that R’ and R” are not both amide.

With regard to claim 22, the Examiner alleges that the claim is indefinite due to the term “tosulate.” In response, to even more clearly recite and distinctly claim Applicants’ invention and to expedite prosecution, claim 22 has been amended to correct a typographical error in spelling, such that the amended claim recites “tosylate.”

With regard to claims 46 and 72, the Examiner alleges that the claims are indefinite due to the recited molecular weights. In response, to expedite prosecution

claims 46 and 72 have been canceled without prejudice to or disclaimer of the subject matter contained therein.

In view of the above, Applicants respectfully submit that the rejections under 35 U.S.C. § 112, second paragraph have been obviated, and thus, respectfully request withdrawal thereof.

***Claim Rejections under 35 U.S.C. § 103(a)***

Claim 72 stands rejected under 35 U.S.C. § 103(a) as allegedly obvious over Haber and claim 72 has been rejected under 35 U.S.C. § 103(a) as allegedly obvious over Haber in view of Rodgers further in view of Folkman. In response, without conceding the propriety of the rejection and and to expedite prosecution, claim 72 has been canceled without prejudice to or disclaimer of the subject matter contained therein. Accordingly, Applicants respectfully submit that the rejections of claim 72 under 35 U.S.C. § 103(a) have been obviated, and thus, respectfully request withdrawal of these rejections.

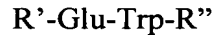
Claims 18, 39, 47, and 72 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Washino in view of Fernandez or Le Noble F. A. Without conceding the propriety of the rejection and to expedite prosecution, claim 18 (upon which claims 39 and 47 depend) has been amended and claim 72 has been canceled without prejudice to or disclaimer of the subject matter contained therein. Applicant respectfully disagrees with the rejection; therefore, this rejection is respectfully traversed.

Washino relates to novel peptides (angiotensin-converting enzyme inhibiting peptides) which are useful for medical and pharmaceutical products for prevention of hypertension, and oral compositions containing said peptides. Washino discloses a peptide having a structure of Ser-Leu-Pro-Lys-Leu-His-Glu-Trp.

Fernandez discloses that angiotensin II has angiogenic properties, in addition to facilitating the activation of preexisting collateral vascular pathways.

Le Noble discloses data that suggests a possible role for antiotensis II as a mediator of vascular growth.

In contrast, independent claim 18 as amended herein relates to a method of inhibiting neovascularization in a subject in need thereof. The method comprises administering to a subject a pharmaceutical preparation comprising a pharmaceutically acceptable carrier and an amount of a compound effective to inhibit neovascularization with the formula of



or pharmaceutically acceptable salts thereof, wherein

R' and/or R'' is absent or

wherein R' represents an alkyl group, an aryl group, an ester, an ether, an anhydride, or mixed alkyl/aryl derivative,

or R', taken together with the alpha-amino group of glutamic acid, represents an amide, or an imide,

R'' represents an alkyl group, an ether, an aryl group, or mixed alkyl/aryl derivative,

or R'', taken together with the carbonyl group of tryptophan represents an imide, an ester, or an anhydride,

wherein R' can also represent an amide bond between the amine of said Glu and the side chain carboxylate of said Glu,

*wherein neither R' nor R'' contains amino acids, and*

wherein the formula weight of said compound is less than 5000 Daltons.

Applicants note that new claim 73 recites a method of inhibiting neovascularization in a subject in need thereof comprising administering a similar, but not identical, compound of the formula of R'-Glu-Trp-R'', *wherein neither R' nor R'' contains amino acids.*

To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP § 2143.

It is respectfully submitted that the presently claimed methods comprise administering compounds R'-Glu-Trp-R'' that are significantly different than the peptide of Washino. As described above, Washino discloses a peptide having a

structure of Ser-Leu-Pro-Lys-Leu-His-Glu-Trp (RJP<sub>8</sub>). In contrast, in the presently claimed methods, compounds of the formula R'-Glu-Trp-R'', wherein *neither R' nor R'' contains amino acids*, are administered. Accordingly, it is respectfully submitted that even if there were some suggestion or motivation to combine the cited references and a reasonable expectation of success, the cited references when combined do not teach or suggest all the claim limitations. Even when combined, Washino in view of Fernandez or Le Noble does not disclose or suggest a method of inhibiting neovascularization in a subject comprising administering a pharmaceutical preparation comprising a pharmaceutically acceptable carrier and an amount of a compound effective to inhibit neovascularization with the formula of

R'-Glu-Trp-R''

or pharmaceutically acceptable salts thereof, wherein *neither R' nor R'' contains amino acids*. Accordingly, it is respectfully submitted that even when the cited art references are combined, they do not teach or suggest all the claim limitations.

For at least the above reasons, the rejections under 35 U.S.C. § 103 should be withdrawn. Such action is respectfully requested.

### ***Double Patenting***

Claims 18, 45, and 48 have been rejected under the judicially created doctrine of obviousness-type double patenting over claim 1 of U.S. Patent No. 5,902,790. Although Applicants believe that the present claims are patentable over the claims of the '790 patent, to facilitate allowable subject matter, Applicants submit herewith a terminal disclaimer over the '790 patent. The filing of a Terminal Disclaimer is not to be construed as an admission of the propriety of the rejection on obvious double patenting. *Quad Environmental Technologies Corp. v. Union Sanitary District*, 946 F.2d 870, 20 USPQ2d 1392 (Fed. Cir. 1991).

In view of the terminal disclaimer submitted herewith, Applicants respectfully submit that this rejection has been obviated.

**CONCLUSION**


Without conceding the propriety of the rejections, the claims have been amended, as provided above, to even more clearly recite and distinctly claim Applicants' invention and to pursue an early allowance. For the reasons noted above, the art of record does not disclose or suggest the inventive concept of the present invention as defined by the claims.

In view of the foregoing remarks, reconsideration of the claims and allowance of the subject application is earnestly solicited. The Examiner is invited to contact the undersigned at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted,

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